Remarks

Claims 11, 14, 16, 33 and 36 were pending in the application. By this amendment, claim 36 is cancelled. Therefore, claims 11, 14, 16, and 33 are now pending.

Amendments to the Specification

The specification has been amended to correct translation errors that occurred when translating the application into English from Japanese. Therefore, no new matter is added by this amendment.

Amendments to the Claims

Support for the amendment to claims 11, 14, and 33 can be found throughout the specification, for example see page 7, lines 6-8; page 11, lines 3-4; and page 12, lines 4-5.

Claims 11, 14, 16 and 33 were amended to clarify that exemplary cardiac muscle disorders include angina pectoris and heart failure. Support for the amendment to claim 16 can be found throughout the specification, for example see page 1, lines 9-15; page 2, lines 23-30 as well as original claims 7, 15, and 22.

Claim Objections

It is concluded in the Office action that claims 16 and 33 are substantially the same as claim 11. Applicants disagree and request reconsideration.

Applicants have amended claim 16 to clarify that a cardiac muscle disorder can include angina pectoris and heart failure.

Claim 33 differs from claim 11 in reciting the phrase "through a catheter". Thus, claim 33 is more limited than claim 11 and is therefore not a substantial duplicate of claim 11.

Applicants therefore request that the objection to the claims be withdrawn.

Rejection under 35 U.S.C. §112, first paragraph

Claim 36 stands rejected under 35 U.S.C. §112, first paragraph. It is asserted that the specification only provides delivery of a nucleic acid to heart tissue under echocardiographic

guidance. It is also concluded that claim 36 includes new matter. Although Applicants disagree (particularly because this claim corresponds to original claim 16), in order to expedite prosecution claim 36 is herein cancelled making the rejection moot.

All of the pending claims were rejected under 35 U.S.C. §112, first paragraph, as not enabled by the specification. It is concluded that the phrase "the nucleic acid molecule comprising a Sendai virus HVJ liposome" is not taught in the specification. Although Applicants disagree, in order to expedite prosecution the phrase has been amended to read "the nucleic acid molecule is encapsulated in a Sendai virus HVJ-liposome".

In view of the amendments and claim cancellation, Applicants request that the 35 U.S.C. §112, first paragraph rejections be withdrawn.

Rejection under 35 U.S.C. §112, second paragraph

Claim 16 has been rejected under 35 U.S.C.§112, second paragraph, as being vague and indefinite. Claim 16 has been amended to depend from claim 11, making this rejection moot. In view of this amendment, Applicants request that the 35 U.S.C.§112, second paragraph rejection be withdrawn.

Rejection under 35 U.S.C. §103(a)

Claims 11, 14, 16, 33 and 35 were rejected under 35 U.S.C. §103(a) as being unpatentable over WO 97/07824, Esakof *et al.*, and Maurice *et al.*, further in view of Stevens *et al.* In the final Office Action mailed on December 18, 2003, page 9, the Office action stated:

> Stevens *et al.* teach a venting catheter system for accessing heart anatomy without the need for a thoracotomy (abstract). They teach the advantage for using such catheter system for a heart procedure without a thoracotomy, "thereby reducing mortality and morbidity, decreasing patient suffering, reducing hospitalization and recovery time, and lowering medical costs relative to previous open-chest procedures" (column 5, lines 56-67). They go on to teach that accurate placement of the catheter could be verified by fluoroscopy or transesophageal echocardiography (column 13, lines 25-27 and column 20, lines 13-24).

In addition, the present Office action on page 8 continues to assert that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by WO 97/07824, Esakof *et al.*, and Maurice *et al.*, by adopting the catheter system taught by Stevens *et al.* in the nucleic acid cardiac delivery procedure with a reasonable expectation of success. Applicants respectfully disagree and request reconsideration.

Stevens *et al.* disclose a venting catheter, system and method for withdrawing blood and other fluids from a patient's heart to facilitate decompressing the heart during cardioplegic arrest and cardiopulmonary bypass, without the need for a thoracotomy and without puncturing the aorta, pulmonary artery, or heart it self (abstract).

Although Stevens *et al.* teach the advantage of no need for a thoracotomy, the venting catheter is used for *withdrawing blood from a patient's heart while the heart is under cardioplegic arrest and the patient is on cardiopulmonary bypass.* The venting catheter is configured to be introduced into a peripheral vein and intralumminally advanced through the right side of the heart and into the pulmonary artery (abstract). Usually, the peripheral vein into which the venting catheter is introduced comprises the internal jugular vein which can be accessed percutaneously or by *surgical cut-down in the patient's neck.* Alternatively, the peripheral vein could be a right subclavian vein, also in the patient's neck, a femoral vein, accessible in the patient's groin, or other peripheral vein of suitable size and location to allow the venting catheter to be positioned intralumminally and advanced into the heart via the inferior vena cava or superior vena cava (column 5, lines 8-14).

In contrast, the claimed invention relates to *non-invasive introduction* of a nucleic acid molecule *directly to a cardiac muscle* of a patient for treating a cardiac muscle disorder. Therefore, one skilled in the art would not have been motivated to use the venting catheter system taught by Stevens *et al.* in gene transfer to a cardiac muscle. Furthermore, as described above, Stevens *et al.* teach that surgical cut-down in the patient's neck can be made. Such method of Stevens *et al.* cannot be said to be non-invasive even if the method does not require thoracotomy.

According to M.P.E.P § 2141, when applying 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the suggested combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) The combination must have a reasonable expectation of success.

Regarding tenet (A), the Office action failed to consider the claimed invention as a whole. Instead, only the elements "catheter" and "without thoracotomy" were considered, each of which the Office action purports to find in the prior art. The purpose and how a catheter is used was disregarded. In determining the differences between the prior art and the claims, the question is not whether the differences *themselves* would have been obvious but whether the claimed invention *as a whole* would have been obvious. See M.P.E.P. § 2141.02 as well as *Stratoflex, Inc. v. Aeroquip Corp*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983) and *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). The mere fact that select aspects of the claimed invention separately exist in the art does not necessarily lead to a conclusion of obviousness.

Regarding tenet (B), the Office action fails to consider the reference as a whole. Sentences from the teachings of the reference were merely selected without considering the reference as a whole. The aspects of the reference other than "catheter" and "without thoracotomy" were ignored. Moreover, the Office action fails to establish a prima facie case of obviousness. There is no teaching in any of the references to suggest or teach the desirability of making the combination. Explicit factual findings on motivation or suggestion to select the claimed invention must be articulated in order to support an obviousness rejection. See In re Dillon, 919 F.2d 688 at 693, 16 USPQ2d 1897 at 1901 (Fed. Cir. 1990). Conclusory statements of "similarity" or "motivation", without any articulated rationale or evidentiary support, do not constitute sufficient factual findings. In other words, to support a conclusion that a claimed invention is obvious, either the references must expressly or impliedly suggest the claimed invention or the PTO must present a convincing line of reasoning as to why one skilled in the art would have found the claimed invention to be obvious in light of the teachings of the references.

The Office action has also failed to satisfy tenet (C). Since clear indications of motivation are missing from the prior art, the motivation to combine can only arise from

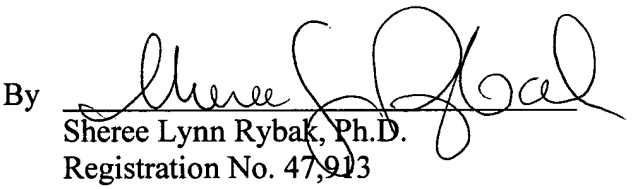
Applicants' own disclosure. In other words, the conclusion of obviousness in this case must be based on improper hindsight reasoning, constituting an ex post analysis that utilizes knowledge gleaned from Applicants' disclosure and not from the prior art. For this reason alone, the suggested combination and conclusion of obviousness are improper and should be withdrawn.

Although Applicants disagree to the reasoning presented in the Office action, to expedite prosecution, claims 11, 14, and 33 have been amended to include the phrase "abdominal lateral cardiac muscle". In view of this amendment and the arguments presented above, Applicants request that the 35 U.S.C.§103(a) rejection be withdrawn.

If the Examiner believes any minor matters remain to be resolved before a Notice of Allowance is issued, she is encouraged to contact the undersigned.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 
Sheree Lynn Rybak, Ph.D.
Registration No. 47,913

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 226-7391
Facsimile: (503) 228-9446